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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)	
D-0021.2-2	

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Signature _____

Typed or printed name _____

Application Number	Filed
10/795,933	March 8, 2004

First Named Inventor: Jan Zavada

Art Unit	Examiner
1635	Dana H. Shin

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)

☑ attorney or agent of record.
Registration number 30,863

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

Signature

Leona L. Lauder
Typed or printed name

415-981-2034
Telephone number

January 15, 2008
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
Submit multiple forms if more than one signature is required, see below*.

☑ *Total of 1 forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Jan Zavada et al.

Serial No. : 10/795,933 Group Art Unit: 1635

Filed : March 8, 2004 Examiner: Dana H. Shin

For : MN Gene and Protein

REQUEST FOR PRE-APPEAL BRIEF CONFERENCE

MAIL STOP AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The following arguments are provided in support of a Request for Pre-Appeal Brief Conference in Application No. 10/795,933.

Claims 31-35 and 39-55 are pending in the application, of which Claims 41-52 have been withdrawn from consideration in view of the 02/15/06 Restriction Requirement. Claims 31-35, 39-40 and 53-55 are currently under examination and are directed to MN antisense oligonucleotide constructs (Claims 31-35 and 53-55) and therapeutic methods using said constructs (Claims 39-40). Applicants respectfully submit that the instant 35 USC §112, ¶1 enablement rejection of Claims 31-35, 39-40 and 53-55 in the Final Office Action mailed from the PTO on November 15, 2007 ["Final Office Action"] is improper and without legal and factual bases.

I. Clear Error Not to Defer to Controlling Precedential DECISION ON APPEAL from Board of Patent Appeals and Interferences ["Board"; Appeal No. 2001-1970; Application No. 08/260,190 (Paper No. 53); mailed July 23, 2003] in Parent Application (now U.S. Patent No. 6,774,117 B1)

Applicants respectfully submit that it was clear error for the Examiner not to defer to the above-identified controlling precedential Decision on Appeal in the parent application, now U.S. Patent No. 6,774,117 B1, over which the pending claims have been terminally disclaimed. That Decision on Appeal overturned an analogous enablement rejection of methods of treating precancer/cancer with MN antisense oligonucleotides in the parent application. Applicants respectfully but emphatically

argued in their 01/04/07 Response at pages 9-37 that the case for enablement of the subject claims is even stronger, than that for the claims of the parent application, which were found by the Board to be enabled.

Whereas the parent claims (in U.S. Patent No. 6,774,117 B1) concern administering simply MN antisense oligonucleotides in a physiologically acceptable carrier, the subject claims concern methods using MN antisense oligonucleotide constructs. Applicants respectfully submit that ones of skill in the art would expect the subject methods using MN antisense constructs to overcome potential drawbacks of using naked antisense nucleic acids (e.g., persistence and stability issues) and to work better than the methods using naked MN antisense oligonucleotides of the parent application (now U.S. Patent No. 6,744,117 B1). [Support for that statement and for the enablement of using MN antisense constructs can be found particularly in the 01/04/07 Response at pages 17-18; and in the 09/12/07 Response at pages 15-16, at pages 18-19, and at pages 20-28.]

The Decision on Appeal in the parent application found "the Gruenert declaration . . . well-reasoned and supported by evidence, either in the specification or in cited prior art references." [Appeal No. 2001-1970 at page 13; copy of Dr. Gruenert's Declaration attached as Appendix I to 01/04/07 Response.] The Examiner in the Final Office Action [at page 8] found Dr. Gruenert's Declaration insufficient to overcome the enablement rejection of the instant claims 31-35, 39-40 and 53-55 because the Declaration concerns methods of treating cancer "*in vivo* comprising administering a naked antisense oligonucleotide. . . . As such, the claimed subject matter . . . essentially differ . . . [from that in the parent application (now U.S. Patent No. 6,774,117 B1)] to which the declaration is directed."

In contrast, the Examiner had initially found Dr. Gruenert's Declaration to be "sufficient to overcome the [enablement] rejection of claims 39-40 based upon . . . [the] declaration [therein] that the *in vitro* data in the instant disclosure sufficiently enable the instantly claimed *in vivo* methods." [02/01/07 Office Action at page 2.] However, the Examiner rejected claims 39-40 at page 3 of the 02/01/07 Office Action under 3 U.S.C. 101 for being "identical in scope with the methods of Claims 1, 10 and 14 of U.S. Patent No. 6,774,117 B1." The Examiner found the remaining claims 31-35 and 53-55 to be in condition for allowance in the 02/01/07 Office Action and in the 10/04/06 Office Action. The Examiner's positions in the 02/01/07 Office Action stand in sharp distinction from the rejection of all the pending claims 31-35, 39-40 and 53-55 as

failing to comply with the § 112, 1st ¶ enablement requirement in the 06/12/07 Office Action and in the Final Office Action.

Applicants respectfully submit that the Examiner had been initially correct in finding Dr. Gruenert's Declaration sufficient to overcome the enablement rejection of claims 39-40 [02/01/07 Office Action at page 2] in accordance with the analogous holding in the Decision on Appeal in the parent application, and that claims 31-35 and 53-55 were in condition for allowance [02/01/07 and 10/04/06 Office Actions]. However, Applicants most respectfully disagree with the Examiner's divergence from the precedential Decision on Appeal in the 06/02/07 Office Action and in the Final Office Action.

II. 35 USC §112, ¶1 Rejection is Without Factual Basis: Relevant Examples in the Disclosure Are Clearly Found for Claimed Subject Matter

Applicants respectfully submit that the instant 35 USC §112, ¶1 enablement rejection is also improper as it is based upon a clear factual error. The Examiner contends that the claimed subject matter would require undue experimentation, as "no relevant working examples . . . are present in the specification as filed." [Final Office Action at page 4.] Applicants respectfully submit that the specification clearly provides sufficient support for the subject matter that is claimed, and therefore the instant 35 USC §112, ¶1 rejection is without a factual basis.

MN protein is an oncogenic protein, primarily expressed in tumor cells. The nucleic acid and amino acid sequences of the human MN gene/protein were provided in the specification. The invention is based on the discoveries that 1) specific MN antisense oligonucleotides (19-mer and 29-mer) inhibited MN expression in human cervical cancer HeLa cells, and 2) MN cDNA antisense constructs inhibited human tumor cell growth in tumorigenic human cell hybrids (formed by fusion of HeLa cells and human fibroblasts), but did not inhibit cell growth in their nontumorigenic counterparts.[1] The claims are directed to MN antisense oligonucleotide constructs, wherein said constructs show antisense activity in human cells, and therapeutic methods using said constructs in humans. However, the instant 35 USC §112, ¶1 rejection is based on the premise that "no relevant working examples . . . are present in the specification as filed,"

1. Two related nontumorigenic and tumorigenic HeLa X fibroblast intraspecific human hybrid cell lines, CGL1 and CGL3 [Stanbridge et al., Somatic Cell Genetics, 7(6): 699-712 (1981)]. Those intraspecific human hybrid cell lines "have very stable chromosome complements." [Ib., page 700.]

and "the only example pertinent to 'antisense' is an *in vitro* example wherein naked antisense oligonucleotides, not vectors comprising antisense oligonucleotides transcribable are transfected into tumor cells." [Final Office Action at page 4; emphasis in the original.] Applicants respectfully but emphatically disagree, submitting that the specification provides highly relevant examples, teaching two specific antisense oligonucleotide sequences that are effective in inhibiting MN gene expression in human tumor cells, and the construction and use of MN antisense vectors that specifically inhibit human hybrid tumor cell growth.

The Examiner also argues that "[t]he specification as originally filed does not provide any practical information as to how to construct the claimed antisense oligonucleotide (19-29 mer) vector. . . ." [Final Office Action at page 4; emphasis in the original.] In response, Applicants respectfully point out that the working MN antisense oligonucleotides and the working MN antisense cDNA construct of the specification, combined with conventional art at the time of the priority date, taught how to make and use antisense oligonucleotide constructs that could overcome difficulties in uptake by cells and were effective at reducing tumor cell growth, particularly in view of Dr. Gruenert's Declaration [see 01/04/07 Response, at pages 9 to 37; and 09/12/07 Response, at pages 13 to 28].

The Examiner is mistaken in her apparent position that testing in organisms, preferably humans, is required for enablement of MN therapeutic antisense oligonucleotide constructs. [See Decision on Appeal, for example, at pages 10-13, and arguments concerning in vitro/in vivo correlation and working examples in 01/04/07 Response at pages 26-37.]

Applicants have also cited prior art that teaches the preparation and utility of constructs expressing antisense oligonucleotides to inhibit the growth of neoplastic human cells as of the priority date [see 09/12/07 Response, at pages 13 to 16]. Applicants respectfully submit that the prior art teachings in combination with the examples in the specification provide sufficient enablement for the claimed antisense constructs and their use.

For the reasons provided above, Applicants respectfully submit that the instant 35 USC §112, ¶1 rejection of Claims 31-35, 39-40 and 53-55 is without a factual basis.

III. 35 USC §112, ¶1 Rejection is Without Legal Basis: Cases Cited by Examiner Inapposite

Applicants respectfully submit that the case law cited by the Examiner is misapplied. For example, the Examiner cites In re Vaeck [20 USPQ2d 1438 at 1445 (Fed. Cir. 1991)] for the ruling that "a rejection under 35 USC 112, first paragraph for lack of enablement was appropriate given the relatively incomplete understanding in the biotechnological field involved. . . ." [Final Office Action, at page 6.] Applicants respectfully point out that the Decision on Appeal in the parent application had found analogous claims enabled, and at page 9 had also cited In re Vaeck (at page 1444).

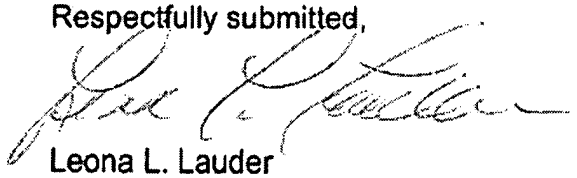
Scott v. Finney, 32 USPQ2d 1115 (Fed. Cir. 1994) cited by the Examiner at the bottom of page 6 of the Final Office Action is inapposite, at least as it applies to a priority contest in an interference context.

Enzo Biochem, Inc. v. Calgene, 52 USPQ2d 1129 (Fed. Cir. 1999) cited at pages 6-7 of the Final Office Action is also inapposite, at least in that the antisense technology therein concerned the regulation of three genes in the prokaryote E. coli versus antisense technology for tomato plants. The principle involved in Enzo was the **unpredictability** of biological technology transfer **between genes** and **between taxonomic kingdoms** (not to mention between genera and/or species), whereas in the instant case, all the antisense claims and working examples are directed to one gene, MN/*CA9*, and one species, human.

IV. Conclusion

For the reasons provided above, Applicants respectfully conclude that the 35 USC 112, ¶ 1 enablement rejection of all the pending claims is improper and without legal or factual bases. In view of the above, Applicants respectfully request a Pre-Appeal Brief Conference to review the subject 35 USC 112, ¶ 1 enablement rejection in the instant application, and that the subject rejection be withdrawn.

Respectfully submitted,



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Dated: January 15, 2008